

Claims

1. A scalable process for the highly selective, high yield separation of nucleic acids, comprising in combination: introduction, enhancement, or stabilization of structural “affinity handles” selectively to either the desired or the undesired moieties or nucleic acid; followed by capture of the undesired (or desired) nucleic acids by techniques which are selective for the characteristics of the affinity handle.
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2. A process according to Claim 1 wherein the handle comprises a structural form selected from the group consisting of single stranded region of nucleic acid, Triplices, Hairpins, Stems, Loops, Cruciforms, G quartets, and modifications to the phosphate backbone.
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3. A process according to Claim 1 wherein the product comprises a moiety that is sensitive to host genomic DNA contamination selective such as single-strandedness in the undesired (or desired) nucleic acids as compared to the usual structure, such as double-strandedness, of the desired (or undesired) nucleic acids.
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4. A process according to Claim 1 wherein the product comprises single-strandedness in the desired product or a moiety that is sensitive to host genomic DNA contamination selective as compared to the structure of the undesired nucleic acids.
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- 25 5. A process according to Claim 4 comprising manufacture of recombinant *Taq* polymerase.

6. A process according to Claim 4 wherein the exposed bases of single-stranded undesired (or desired) nucleic acids facilitate a separation step selected from the group comprising: immobilized metal affinity

5 chromatography (IMAC), immobilized single-stranded DNA binding (SSB) protein, immobilized nucleic acids (poly-dT, poly-dU, or specific sequences), and the use of peptide nucleic acids (PNAs).

7. A process according to Claim 1 comprising introducing single
10 strandedness as a handle.

8. A process according to Claim 1 occurring after another thermally based process (such as heat-based microbial lysis), in which a nucleic acid contaminant (such as genomic DNA) is rapidly cooled to below 65°C and is
15 captured by an affinity method.

9. A process according to Claim 1 performed after another alkali based process (such as alkaline lysis), in which genomic DNA or other nucleic acid contaminant) is rapidly neutralized and is captured by an affinity method.

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10. A process according to Claim 1 comprising a step for introducing handles selected from the group comprising: selective thermal denaturation and renaturation, alkaline denaturation, the use of chaotropic agents, the use of restriction enzymes yielding single-stranded overhangs, the use of
25 oligonucleotide dTs, single-stranded DNA binding proteins, minerals, and the use of primers or other nucleic acid fragments such as complementary

DNA nucleic acids to facilitate capture and separation of the undesired (or desired) nucleic acid from the desired (or undesired) nucleic acids.

11. A process according to Claim 1 wherein other plasmid isoforms selected from the group consisting of open circular (“nicked”) and linear are 5 selectively removed from the desired supercoiled plasmid DNA.
12. A process according to Claim 9 wherein other plasmid isoforms selected from the group consisting of open circular and linear are selectively removed from supercoiled plasmid DNA.
14. A process according to Claim 1 in which the separation is achieved by 10 adsorption on chelated metal.
15. A process according to Claim 1 in which the separation is achieved using multi-channel plates.
16. A process according to Claim 1 in which the separation is achieved using spin columns.
- 15 17. A process according to Claim 1 in which the separation is achieved using magnetic particles.
18. A process according to Claim 1 in which the separation of multiple samples is achieved in parallel fashion.
19. A process according to Claim 1 in which the product comprises a 20 protein.
- 40* [20. A process according to Claim 1 in which the desired product is a plasmid.]

✓ [21. A process according to Claim 1 in which the desired product is genomic DNA.]

✓ [22. A process according to Claim 1 in which the desired product is RNA.]

[23. A process according to Claim 1 in which the capture method is RPC.]

✓ 5 [24. A process according to Claim 1 in which the capture method is HIC.]

20, 25. All inventions substantially as described herein.